

Epigenetic mechanisms that enforce pluripotency in embryonic stem cells

Grant Award Details

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Grant Type: Basic Biology V

Grant Number: RB5-07025

Project Objective: To understand how the 3D topology of genomes differ in hESCs and hiPSCs and how reprogramming is associated with the large-scale nuclear repositioning of genes during the transition from the lymphoid or myeloid cell to the iPSC stage

Investigator:

Name:	Cornelis Murre
Institution:	University of California, San Diego
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell, iPS Cell

Award Value: \$1,160,997

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 2

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Reporting Period: Year 3

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Grant Application Details

Application Title: Epigenetic mechanisms that enforce pluripotency in embryonic stem cells

Public Abstract: Embryonic stem (ES) cells have the unique ability to self-renew while maintaining a pluripotent state. They can readily be differentiated into all cell types upon exposure to the appropriate stimuli. The differentiation of ES cells into specialist cell types involves the activation of lineage-specific programs of gene expression and the silencing of genes that promote pluripotency. These changes are now well known to include epigenetic modifications such as DNA methylation and deposition of distinct histone marks across the genome. However, much remains to be learned as to how ES cells differ from differentiated progeny. In particular, it has remained unclear as to how the 3D-structures of the ES cell genome change upon developmental progression into a fully committed cell type and during reprogramming. Thus, we are now faced with the fundamental question as to how the 3D-structures of human ES cell genomes differ from that of differentiated progeny and how such differences relate to the establishment and maintenance of pluripotency versus differentiation. This is the focus of the studies proposed in this application.

Statement of Benefit to California: Our studies would provide insights into the mechanisms that underpin the abilities of human embryonic stem cells to self renew and to differentiate into specific cell lineages. This research will serve as a foundation for understanding the basic properties of human embryonic stem cells and differentiated progeny. Understanding and modifying the properties of stem cells would directly impact novel approaches that are being developed to study stem cell models of many types of diseases and regenerative medicine. It would also permit the development of new avenues for the diagnosis and treatment of human disease and help to maintain the position of California as a leader in basic and applied biomedical research.

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